FILE 'AGRICOLA, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHDS, CABA, CANCERLIT, CAPLUS, CEABA, CIN, CONFSCI, DGENE, EMBASE, ESBIOBASE, FSTA, GENBANK, JICST-EPLUS, LIFESCI, MEDLINE, NTIS, PROMT, SCISEARCH, TOXLINE'
ENTERED AT 10:48:51 ON 09 NOV 2000

L1	293784	S REGULAT? (3A) (GENE EXPRESSION)
L2	4361	S MOLECUL? (3A) SWITCH
L3	365950	S DNA (3A) BIND?
L4	168	S L2 (S) L3
L5	12	S L1 (L) L4
L6	4	DUP REM L5 (8 DUPLICATES REMOVED)
L7	57706	S INDUC? (S) L3
L8	35	S L7 (S) L2
L9	1	S L1 (L) L8
L10	8	DUP REM L8 (27 DUPLICATES REMOVED)
L11	9629	S GENE (2A) EXPRESSION (2A) SYSTEM
L12	127	S L11 (S) L7
L13	0	S L12 (L) L2
L14	101	S L12 (L) REGULAT?
L15	30	DUP REM L14 (71 DUPLICATES REMOVED)

L6 ANSWER 1 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 2000:409232 BIOSIS
DOCUMENT NUMBER: PREV200000409232
TITLE: Gene regulation by thyroid hormone.
AUTHOR(S): Wu, Yifei (1); Koenig, Ronald J. (1)
CORPORATE SOURCE: (1) Division of Endocrinology and Metabolism and Program in
Cellular and Molecular Biology, University of Michigan Medical Center, 1150 West Medical Center Drive, 5560 MSRB-II, Ann Arbor, MI, 48109-0678 USA
SOURCE: Trends in Endocrinology and Metabolism, (August, 2000) Vol.
11, No. 6, pp. 207-211. print.
ISSN: 1043-2760.
DOCUMENT TYPE: General Review
LANGUAGE: English
SUMMARY LANGUAGE: English
AB **Regulation** of **gene expression** by thyroid hormones (T3, T4) is mediated via thyroid hormone receptors (TRs). TRs are **DNA-binding** transcription factors that function as **molecular switches** in response to ligand. TRs can activate or repress gene transcription depending on the promoter context and ligand-binding status. In most cases, in the absence of ligand, TRs interact with a corepressor complex containing histone deacetylase activity, which actively inhibits transcription. The binding of ligand triggers a conformational change in the TR that results in the replacement of the corepressor complex by a coactivator complex containing histone acetyltransferase activity, through which the chromatin structure is remodeled, thereby leading to activation of transcription. In addition, the finding that several TR-interacting coregulators act more directly on the basal transcriptional machinery suggests that mechanisms independent of histone acetylation and deacetylation also are involved in TR action.

L6 ANSWER 2 OF 4 CANCERLIT DUPLICATE 2
ACCESSION NUMBER: 1998048260 CANCERLIT
DOCUMENT NUMBER: 98048260
TITLE: Exploring the role of homeobox and zinc finger proteins in pancreatic cell proliferation, differentiation, and apoptosis.
AUTHOR: Urrutia R
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Mayo Clinic, Rochester, MN, USA.
SOURCE: INTERNATIONAL JOURNAL OF PANCREATOLOGY, (1997). Vol. 22, No. 1, pp. 1-14.
Journal code: IJP. ISSN: 0169-4197.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 98048260
ENTRY MONTH: 199802
AB Transcription factors are **DNA binding** proteins that **regulate gene expression** in response to a large variety of extracellular stimuli, and thereby act as key **molecular switches** for controlling cell differentiation,

proliferation, and apoptosis. During the last decade, a myriad of these proteins have been identified and classified into different structural families, including homeobox, zinc finger, leucine zipper, and helix-loop-helix transcription factors. Members of the homeobox and zinc finger superfamilies are among the best-characterized transcription factors known to act as potent regulators of normal development in organisms ranging from insects to humans. In addition, mutations or aberrant expression in genes encoding these proteins can result in neoplastic transformation in several different cell types, further supporting their role as "guardians" of normal cell growth and differentiation. Therefore, the purpose of this article is to review this field of research with a particular emphasis on the role of homeobox- and zinc finger-containing transcription factors in pancreatic cell growth, cell differentiation, and apoptosis. The potential participation of these proteins in neoplastic transformation is also discussed.

L6 ANSWER 3 OF 4 BIOTECHDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-01365 BIOTECHDS
TITLE: Steroid hormone receptor mutant and molecular switch; useful in senile dementia, Parkinson disease, etc., gene therapy
PATENT ASSIGNEE: Baylor-Coll.Med.
PATENT INFO: WO 9323431 25 Nov 1993
APPLICATION INFO: WO 1993-US4399 11 May 1993
PRIORITY INFO: US 1992-939246 2 Sep 1992; US 1992-882771 14 May 1992
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 1993-386482 [48]
AN 1994-01365 BIOTECHDS
AB A mutant steroid hormone receptor (I) protein capable of distinguishing a
hormone agonist from an antagonist is claimed. Also claimed are: (1) a plasmid containing (I), especially plasmid UP-1, plasmid YEphPR-A879, plasmid YEphPR-A891, plasmid YEphPR-B891, plasmid YEphPR-B879, plasmid phPR-A879, plasmid phPR-A891, plasmid phPR-B879 and plasmid phPR-B891; (2) a transfected cell or cell line (Saccharomyces cerevisiae, HeLa, CV-1, COSM6, HepG2, CHO, Ros17.2, Sf9, Drosophila, butterfly or bee); (3)
a method for determining antagonist or agonist activity of a compound using the transfected cells; (4) a method for determining an endogenous ligand for (I); (5) an endogenous ligand for (I); (6) a modified progesterone receptor; (7) a composition containing plasmid UP-1; (8) a **molecular switch** (VP-16 or TAF-1 transcription region attached to (I) including a GAL-4 **DNA binding** domain and a modified ligand binding domain) for **gene expression regulation** in gene therapy, transgenic animals or transgenic plants; (9) a method for **regulating gene expression**; and (10) a **molecular switch** composition. (52pp)

L6 ANSWER 4 OF 4 CANCERLIT
ACCESSION NUMBER: 90662236 CANCERLIT
DOCUMENT NUMBER: 90662236
TITLE: TRANSACTIVATION OF LATENT EPSTEIN-BARR VIRUS: EVIDENCE FOR AN AP-1/FOS-LIKE FAMILY OF CELLULAR AND VIRAL REGULATORY PROTEINS IN THE TISSUE SPECIFIC ACTIVATION OF EBV.
AUTHOR: Lieberman P M
CORPORATE SOURCE: Johns Hopkins Univ.
SOURCE: Diss Abstr Int [B], (1990). Vol. 50, No. 7, pp. 2723. ISSN: 0419-4217.
DOCUMENT TYPE: (THESIS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199005
AB Epstein-Barr Virus (EBV) is a human lymphotropic herpesvirus associated

with Burkitt's lymphoma and nasopharyngeal carcinoma. Like other herpesviruses, EBV establishes and maintains a latent infection which persists for the duration of the host's life. To better understand the molecular mechanism regulating the switch between the latent and lytic cycle of EBV, I have examined the ability of 'immediate early' genes of the lytic cycle to function as regulatory genes in transient expression assays. In chapters I and II, I have compared the functional differences of the MS 'promiscuous' transactivator with the Z specific transactivator, which has the unique capacity to induce the viral lytic cycle. I showed that one EBV promoter, derived from DS-L and regulating the TPA inducible Not-1 repeat transcript, responded specifically to the Z mediated transactivation. The specific interaction of the Z transactivator with the Not-1 Repeat Promoter (NRP) is characterized on genetic and biochemical levels in chapters III and IV. NRP consists of a VERO cell specific promoter and a B-cell specific enhancer element which are both responsive to Z transactivation. Cellular factors derived from B-cell nuclear extracts indicated multiple interactions occur in these response regions, with a CCAAT like element mediating activation in the promoter sequences and a 12 by palindrome binding factor interacting with the enhancer sequences. Finally, affinity purified Z fusion protein synthesized in bacteria was shown to bind directly to the Z responsive sequences of the enhancer element. The Z protein sequence shows significant homology to the proto-oncogene c-jun and c-fos. The cognate binding site for the Z protein appears to be one bp diverged from the published AP-1 binding site. I found that the Z protein transactivates the TRE element in a lymphocyte specific manner, and bound the same sequence by gel mobility shift analysis. We conclude that an AP-1 like activator protein encoded in EBV regulates lytic cycle gene expression by binding directly to DNA and interacting with cellular transcription factors in a tissue specific manner. (Full text available from University Microfilms International, Ann Arbor, MI, as Order No. AAD89-23715)

L10 ANSWER 1 OF 8 TOXLINE
ACCESSION NUMBER: 1999:74041 TOXLINE
DOCUMENT NUMBER: FEDRIP-1999-06411416
TITLE: Age-Dependent Changes in Cellular Responses to inflamation and Stress.
AUTHOR: Jurivich D A
CORPORATE SOURCE: Department of Veterans Affairs/Medical Center, Chicago, IL
Department of Veterans Affairs/Research and Development (15), 810 Vermont Ave. N.W., Washington, D.C.
CONTRACT NUMBER: VA 00212646
SOURCE: (1999). FEDRIP DATABASE, NATIONAL TECHNICAL INFORMATION SERVICE (NTIS).
FILE SEGMENT: FEDRIP
LANGUAGE: Unavailable
ENTRY MONTH: 199904

AB RPROJ/FEDRIP TRANSCRIPTION FACTORS; SIGNAL TRANSDUCTION; INFLAMMATION; AGING OBJECTIVES: The long term goal is to reverse age-dependent losses in cellular function related to inflammation. During inflammation, lymphocytes and other white blood cells have to protect themselves from injury and death response is to facilitate cellular repair and to protect cells from further injury and death. One method to achieve this effect is to **induce** heat shock gene expression. Increased hs gene expression enhances the production of heat shock proteins or stress chaperones. These proteins prevent cell injury and death by protecting nascent proteins, disaggregating damaged proteins and preserving protein kinase activity. The cellular stress response involves at least one **molecular switch** mediated by the transcriptor of hs genes, heat shock transcription factor (HSF1). An inflammatory mediator, arachidonate, triggers HSF1, and aging is known to alter the activation of this important transcription factor. Thus, the goal of this project is to understand how archidonate triggers HSF1 and how lymphocytes from normal, elderly human donors manifest defective activation of HSF1. METHODS: Molecular and biochemical assays will be used to determine if HSF1 contains a lipid-sensitive domain. Arachidonate and other types of lipids will be assessed for their potency in activating HSF1 and known in vivo activators. of archidonate metabolism will be tested for their contribution towards HSF1 activation. Based on this information, lymphocytes from aged donors will be analyzed for their response to archidonate employing electromobility shift assay of HSF1 **DNA binding**. Archidonate-**induced** HSF1 will be further assessed by lipid-HSF1 binding assays. The multimeric state of HSF1 will be characterized by pore gradient analysis and western blotting. Finally, a putative inhibitor of HSF1 multimerization will be evaluated and partially characterized. FINDINGS: Aging causes defective activation of heat shock gene expression. This is due to defective **induction** of HSF1 at the level of **DNA binding** and multimerization. HSF1 phosphorylation overall does not seem to be affected by age, but this does not preclude single serine residues becoming phosphorylated and acting as negative regulators of HSF1 function. PLA2 appears to partially activate HSF1 via multimerization but not phoshorylation. This is surprising given the potent effects of archidonate in causing both HSF1 multimerization phosphorylation. An additional surprise is that macrophages are insensitive to the effects of PLA2, unlike lymphocytes. CLINICAL RELEVANCE: Understanding age-dependent

changes in molecular response to inflammation is clinically important for several reasons: 1.) elderly have poor responses to inflammation as evident by higher infection rates (both chronic and acute) and poorer outcomes in this population, 1.) defective responses to inflammation are thought to be associated with carcinogenesis and cancer is disproportionately represented in the aging population, 3) autoimmune problems such as drug-**induced** lupus disproportionately affect the elderly, and lastly, 4.) ischemia **induces** inflammation and altered responses with aging likely contribute to poor tissue viability and loss of function. Thus, understanding basic responses of lymphocytes to inflammation with aging has important implications for other organs at risk Also noted, is the new hypothesis that Alzheimer's disease has an inflammatory component, and the lymphocyte model of senescence and stress responses will have important implication for understanding defects in aged neuronal cells at risk for injury and death. By understanding how age alters HSF1 regulation and the cellular stress response, strategies can be developed to intervene and reconstitute the stress response. These clinical interventions entail pharmacological and gene therapy strategies.

This study is closed at VA Chicago Health Care System, Lakeside Division.

L10 ANSWER 2 OF 8 CANCERLIT DUPLICATE 1

ACCESSION NUMBER: 1999370008 CANCERLIT
DOCUMENT NUMBER: 99370008
TITLE: Switch recombination in a transfected plasmid occurs preferentially in a B cell line that undergoes switch recombination of its chromosomal Ig heavy chain genes.
AUTHOR: Stavnezer J; Bradley S P; Rousseau N; Pearson T; Shanmugam A; Waite D J; Rogers P R; Kenter A L
CORPORATE SOURCE: Department of Molecular Genetics and Microbiology, Program in Immunology and Virology, University of Massachusetts Medical School, Worcester 01655, USA.
janet.stavnezer@banyan.ummed.edu
CONTRACT NUMBER: RO1 AI23283 (NIAID)
RO1 GM 57078 (NIGMS)
T32 AI07349 (NIAID)
SOURCE: JOURNAL OF IMMUNOLOGY, (1999). Vol. 163, No. 4, pp. 2028-40.
Journal code: IFB. ISSN: 0022-1767.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Abridged Index Medicus Journals; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99370008
ENTRY MONTH: 199910

AB Ab class switching is **induced** upon B cell activation in vivo by immunization or infection or in vitro by treatment with mitogens, e. g. LPS, and results in the expression of different heavy chain constant region (CH) genes without a change in the Ab variable region. This DNA recombination event allows Abs to alter their biological activity while maintaining their antigenic specificity. Little is known about the **molecular** mechanism of **switch** recombination. To attempt to develop an assay for enzymes, **DNA binding** proteins, and **DNA** sequences that mediate switch recombination, we have constructed a plasmid DNA substrate that will undergo switch recombination upon stable transfection into the surface IgM+ B cell line (I.29 mu), a cell line capable of undergoing switch recombination of its endogenous genes. We demonstrate that recombination occurs between the two switch regions of the plasmid, as assayed by PCRs across the integrated plasmid switch regions, followed by Southern blot hybridization. Nucleotide sequence analysis of the PCR products confirmed the occurrence of S mu-S alpha recombination in the plasmid. Recombination of the plasmid in I.29

mu cells does not require treatment with **inducers** of switch recombination, suggesting that recombinase activity is constitutive in I.29 mu cells. R[redacted]mbination does not require hig[redacted]evels of transcription
across the switch regions of the plasmid. Fewer recombination events are detected in four different B and T cell lines that do not undergo switch recombination of their endogenous genes.

L10 ANSWER 3 OF 8 AGRICOLA DUPLICATE 2
ACCESSION NUMBER: 2000:9880 AGRICOLA
DOCUMENT NUMBER: IND22020966
TITLE: Modulation of GT-1 DNA-binding activity by calcium-dependent phosphorylation.
AUTHOR(S): Marechal, E.; Hiratsuka, K.; Delgado, J.; Nairn, A.; Qin, J.; Chait, B.T.; Chua, N.H.
CORPORATE SOURCE: Rockefeller University, New York, NY.
AVAILABILITY: DNAL (QK710.P62)
SOURCE: Plant molecular biology, June 1999. Vol. 40, No. 3. p.
373-386
Publisher: Dordrecht : Kluwer Academic Publishers.
CODEN: PMBIDB; ISSN: 0167-4412
NOTE: Includes references
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English
AB The analysis of pea rbcS-3A promoter sequence showed that BoxII was necessary for the control of rbcS-3A gene expression by light. GT-1, a **DNA-binding** protein that interacts with BoxII in vitro, is a good candidate for being a light-modulated **molecular switch** controlling gene expression. However, the relationship between GT-1 activity and light-responsive gene activation still remains hypothetical. Because no marked de novo synthesis was detected after light
treatment, light may **induce** post-translational modifications of GT-1 such as phosphorylation or dephosphorylation. Here, we show that recombinant GT-1 (hGT-1) of Arabidopsis can be phosphorylated by various mammalian kinase activities in vitro. Whereas phosphorylation by casein kinase II had no apparent effect on hGT-1 **DNA binding**, phosphorylation by calcium/calmodulin kinase II (CaMKII) increased the binding activity 10-20-fold. Mass spectrometry analyses of the phosphorylated hGT-1 showed that amongst the 6 potential phosphorylatable residues (T86, T133, S175, T179, S198 and T278), only T133 and S198 are heavily modified. Analyses of mutants altered at T86, T133, S175, T179, S198 and T278 demonstrated that phosphorylation of T133 can account for most of the stimulation of **DNA-binding** activity by CaMKII, indicating that this residue plays an important role in hGT-1/BoxII interaction. We further showed that nuclear GT-1 **DNA -binding** activity to BoxII was reduced by treatment with calf intestine phosphatase in extracts prepared from light-grown plants but not
from etiolated plants. Taken together, our results suggest that GT-1 may act as a **molecular switch** modulated by calcium-dependent phosphorylation and dephosphorylation in response to light signals.

L10 ANSWER 4 OF 8 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 3
ACCESSION NUMBER: 1998:480019 BIOSIS
DOCUMENT NUMBER: PREV199800480019
TITLE: Identification of a copper-induced intramolecular interaction in the transcription factor Mac1 from Saccharomyces cerevisiae.
AUTHOR(S): Jensen, Laran T.; Winge, Dennis R. (1)
CORPORATE SOURCE: (1) Dep. Biochemistry, Univ. Utah Health Science Cent.,

Salt Lake City, UT 84132 USA
SOURCE: EMBO (European Molecular Biology Organization) Journal, ([redacted]t. 15, 1998) Vol. 17, No. 18, [redacted] 5400-5408.
ISSN: 0261-4189.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Mac1 mediates copper (Cu)-dependent expression of genes involved in high-affinity uptake of copper ions in Saccharomyces cerevisiae. Mac1 is a transcriptional activator in Cu-deficient cells, but is inhibited in Cu-replete cells. Mac1 resides within the nucleus in both Cu-deficient and Cu-loaded cells. Cu inhibition of Mac1 appears to result from binding of eight copper ions within a C-terminal segment consisting of two Cys-rich motifs. In addition, two zinc ions are bound within the N-terminal **DNA-binding** domain. Only 4-5 mol. eq. Cu are bound to a mutant Mac1 (His279Gln substitution) that is impervious to Cu inhibition. The CuMac1 complex is luminescent, indicative of copper bound in the Cu(I) state. Cu binding **induces** a **molecular switch** resulting in an intramolecular interaction in Mac1 between the N-terminal **DNA-binding** domain and the C-terminal activation domain. This allosteric interaction is Cu dependent and is not observed when Mac1 contained the mutant His279Gln substitution. Fusion of the minimal **DNA-binding** domain of Mac1 (residues 1-159) to the minimal Cu-binding activation domain (residues 252-341) yields a functional Cu-regulated transcriptional activator. These results suggest that Cu repression of Mac1 arises from a Cu-**induced** intramolecular interaction that inhibits both **DNA binding** and transactivation activities.

L10 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
ACCESSION NUMBER: 1996:234367 CAPLUS
DOCUMENT NUMBER: 124:286207
TITLE: Regulation of MHC class II genes: lessons from a disease
AUTHOR(S): Mach, Bernard; Steimle, Viktor; Martinez-Soria, Eduardo; Reith, Walter
CORPORATE SOURCE: Department Genetics, University Geneva Medical School, Geneva, 1211, Switz.
SOURCE: Annu. Rev. Immunol. (1996), 14, 301-31
CODEN: ARIMDU; ISSN: 0732-0582
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 138 refs. Precise regulation of major histocompatibility complex class II (MHC-II) gene expression plays a crucial role in the control of the immune response. A major breakthrough in the elucidation of the mol. mechanisms involved in MHC-II regulation has recently come from the study of patients that suffer from a primary immunodeficiency resulting from regulatory defects in MHC-II expression. A genetic complementation cloning approach has led to the isolation of CIITA and RFX5, two essential MHC-II gene transactivators. CIITA and RFX5 are mutated in these patients, and the wild-type genes are capable of correcting their defect in MHC-II expression. The identification of these regulatory factors has furthered the understanding of the mol. mechanisms that regulate MHC-II genes. CIITA was a non-**DNA binding** transactivator that functions as a **mol. switch** controlling both constitutive and **inducible** MHC-II expression. The finding that RFX5 is a subunit of the nuclear RFX-complex has confirmed that a deficiency in the binding of this complex is indeed the mol. basis for MHC-II deficiency in the majority of patients. Furthermore, the study of RFX has demonstrated that MHC-II promoter activity is dependent on the binding of higher-order complexes that are

formed by highly specific cooperative binding interactions between certain MHC-II promoter-binding proteins. Two of these proteins belong to families of which the other members, although capable of binding to the same DNA motifs, are probably not directly involved in the control of MHC-II expression. Finally, the facts that CIITA and RFX5 are both essential and highly specific for MHC-II genes make possible novel strategies designed to achieve immunomodulation via transcriptional intervention.

L10 ANSWER 6 OF 8 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 94069421 MEDLINE
DOCUMENT NUMBER: 94069421
TITLE: Activation of muscle-specific transcription by myogenic helix-loop-helix proteins.
AUTHOR: Olson E
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, University of Texas, M. D. Anderson Cancer Center, Houston 77030..
SOURCE: SYMPOSIA OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY, (1992) 46
331-41. Ref: 38
Journal code: VGF. ISSN: 0081-1386.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403

AB Myogenin is a muscle-specific transcription factor that acts as a **molecular switch** to **induce** myogenesis. Myogenin shares homology with MyoD and other myogenic regulatory proteins within a basic region and helix-loop-helix (HLH) motif that mediate **binding** to a conserved **DNA** sequence (CANNTG) present in the regulatory regions of numerous muscle-specific genes. Binding of myogenin and other members of the MyoD family to DNA can be augmented upon heterodimerization with the widely expressed HLH protein E12. We have used the muscle creatine kinase (MCK) enhancer as a target to study the mechanism whereby myogenin activates muscle-specific transcription. Full activity of the MCK enhancer requires cooperative interactions between myogenin (or other myogenic HLH proteins that bind the same site) and a complex array of ubiquitous and cell type-specific nuclear factors. To define the domains of myogenin responsible for sequence-specific **DNA binding**, activation of muscle-specific transcription, and cooperativity with other transcription factors, we have generated an extensive series of mutants by site-directed mutagenesis and domain swapping. These mutants have revealed strong transcriptional activation domains in the N- and C-termini of myogenin that rely on a specific amino acid sequence within the **DNA binding** domain for activity. Myogenin's ability to **induce** muscle-specific transcription is subject to negative regulation by growth factor and oncogenic signals. Mechanisms through which growth signals may repress myogenin function are discussed.

L10 ANSWER 7 OF 8 CANCERLIT
ACCESSION NUMBER: 90662236 CANCERLIT
DOCUMENT NUMBER: 90662236
TITLE: TRANSACTIVATION OF LATENT EPSTEIN-BARR VIRUS: EVIDENCE FOR AN AP-1/FOS-LIKE FAMILY OF CELLULAR AND VIRAL REGULATORY PROTEINS IN THE TISSUE SPECIFIC ACTIVATION OF EBV.
AUTHOR: Lieberman P M

CORPORATE SOURCE: Johns Hopkins Univ.
SOURCE: Diss Abstr Int [B], (1990). Vol. 50, No. 7, pp. 2723.
ISSN: 0419-4217.
DOCUMENT TYPE: (THESIS)
FILE SEGMENT: ICDB
LANGUAGE: English
ENTRY MONTH: 199005

AB Epstein-Barr Virus (EBV) is a human lymphotropic herpesvirus associated with Burkitt's lymphoma and nasopharyngeal carcinoma. Like other herpesviruses, EBV establishes and maintains a latent infection which persists for the duration of the host's life. To better understand the **molecular** mechanism regulating the **switch** between the latent and lytic cycle of EBV, I have examined the ability of 'immediate early' genes of the lytic cycle to function as regulatory genes in transient expression assays. In chapters I and II, I have compared the functional differences of the MS 'promiscuous' transactivator with the Z specific transactivator, which has the unique capacity to **induce** the viral lytic cycle. I showed that one EBV promoter, derived from DS-L and regulating the TPA **inducible** Not-1 repeat transcript, responded specifically to the Z mediated transactivation. The specific interaction of the Z transactivator with the Not-1 Repeat Promoter (NRP) is characterized on genetic and biochemical levels in chapters III and IV.

NRP consists of a VERO cell specific promoter and a B-cell specific enhancer element which are both responsive to Z transactivation. Cellular factors derived from B-cell nuclear extracts indicated multiple interactions occur in these response regions, with a CCAAT like element mediating activation in the promoter sequences and a 12 by palindrome binding factor interacting with the enhancer sequences. Finally, affinity purified Z fusion protein synthesized in bacteria was shown to bind directly to the Z responsive sequences of the enhancer element. The Z protein sequence shows significant homology to the proto-oncogene c-jun and c-fos. The cognate binding site for the Z protein appears to be one bp diverged from the published AP-1 binding site. I found that the Z protein transactivates the TRE element in a lymphocyte specific manner, and bound the same sequence by gel mobility shift analysis. We conclude that an AP-1 like activator protein encoded in EBV regulates lytic cycle gene expression by **binding** directly to **DNA** and interacting with cellular transcription factors in a tissue specific manner. (Full text available from University Microfilms International, Ann Arbor, MI, as Order No. AAD89-23715)

L10 ANSWER 8 OF 8 CANCERLIT DUPLICATE 6
ACCESSION NUMBER: 90114753 CANCERLIT
DOCUMENT NUMBER: 90114753
TITLE: Immediate-early genes, kindling and long-term potentiation.
AUTHOR: Dragunow M; Currie R W; Faull R L; Robertson H A; Jansen K
CORPORATE SOURCE: Department of Anatomy, School of Medicine, University of Auckland, New Zealand.
SOURCE: NEUROSCIENCE AND BIOBEHAVIORAL REVIEWS, (1989). Vol. 13, No. 4, pp. 301-13.
Journal code: OA7. ISSN: 0149-7634.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 90114753
ENTRY MONTH: 199003

AB The mechanism(s) by which long-term changes are **induced** and maintained in the nervous system are poorly understood. Kindling is an

example of a permanent change in brain function that results from repeated elicitation of seizures. Recently, a class of genes called "immediate-early genes" that were previously thought to be only involved in cell division, differentiation and perhaps neoplasia have been shown to be rapidly and transiently **induced** in adult neurons following afterdischarges, ECS and chemically-evoked seizures. The products of these genes (e.g., FOS, JUN) are **DNA-binding** proteins and it is thought that they alter, perhaps in a coordinate fashion, the transcription of "late-effector genes." These late genes may code for enzymes, neuropeptides, receptors, ion channels, structural proteins, growth factors, etc. that may cause permanent biochemical and/or morphological changes in the brain that give rise to the kindled state. Thus, these early genes may act as **molecular switches** turning on a plasticity (kindling) program in neurons in a fashion similar to their **induction** of developmental programs in dividing cells.

L15 ANSWER 1 OF 30 BIOTECHDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI New transactivator containing mutant tetracycline repressor, useful e.g. as pharmaceutical and for regulation of gene expression, has amino acids exchange at selected sites;
method is useful for constructing mutant transactivator via plasmid pCM190-GFP from Saccharomyces cerevisiae
AU Hillen W
AN 2000-10150 BIOTECHDS
AB A mutant transactivator (A) containing a tetracycline repressor (TetR) is
claimed. (A) includes at least one amino acid (aa) exchange in the **DNA binding** region, especially position 9, one aa
exchange in helix 4, particularly at position 56, optionally additional exchange at 148 or 179, and optionally at least one exchange at positions
71, 95, 101 and 102. (A) includes the herpes simplex virus protein VP16 and activates expression, depending on the presence of low mol.wt. **inducers**. (A) are used in pharmaceuticals, transgenic organisms, **expression systems** or **gene-regulatory systems** and provide **gene expression** that is **regulated** by low mol.wt. **inducers**, particularly
tetracyclines. (A) give, in yeast, mammalian cells or plants, higher **induction** rates than known reverse transactivators (rtTA). They provide a low basal level of expression, eliminating the need for a repressor, and may be **induced** specifically. (49pp)

L15 ANSWER 2 OF 30 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 1
TI The ciliary neurotrophic factor and its receptor, CNTFR.alpha..
SO Pharmaceutica Acta Helvetiae, (2000) 74/2-3 (265-272).
Refs: 62
ISSN: 0031-6865 CODEN: PAHEAA
AU Sleeman M.W.; Anderson K.D.; Lambert P.D.; Yancopoulos G.D.; Wiegand S.J.
AB Ciliary neurotrophic factor (CNTF) is expressed in glial cells within the central and peripheral nervous **systems**. CNTF stimulates **gene expression**, cell survival or differentiation in a variety of neuronal cell types such as sensory, sympathetic, ciliary and motor neurons. In addition, effects of CNTF on oligodendrocytes as well as
denervated and intact skeletal muscle have been documented. CNTF itself lacks a classical signal peptide sequence of a secreted protein, but is thought to convey its cytoprotective effects after release from adult glial cells by some mechanism **induced** by injury. Interestingly, mice that are homozygous for an inactivated CNTF gene develop normally and
initially thrive. Only later in adulthood do they exhibit a mild loss of motor neurons with resulting muscle weakness, leading to the suggestion that CNTF is not essential for neural development, but instead acts in response to injury or other stresses. The CNTF receptor complex is most closely related to, and shares subunits with the receptor complexes for interleukin-6 and leukemia inhibitory factor. The specificity conferring .alpha. subunit of the CNTF complex (CNTFR.alpha.), is extremely well conserved across species, and has a distribution localized predominantly to the nervous system and skeletal muscle. CNTFR.alpha. lacks a conventional transmembrane domain and is thought to be anchored to the cell membrane by a glycosyl-phosphatidylinositol linkage. Mice lacking CNTFR.alpha. die perinatally, perhaps indicating the existence of a second
developmentally important CNTF-like ligand. Signal transduction by CNTF

requires that it bind first to CNTFR.alpha., permitting the recruitment of gp130 and LIFR.b[redacted]., forming a tripartite recept[redacted] complex. CNTF-**induced** heterodimerization of the .beta. receptor subunits leads to tyrosine phosphorylation (through constitutively associated JAKs), and the activated receptor provides docking sites for SH2-containing signaling molecules, such as STAT proteins. Activated STATs dimerize and translocate to the nucleus to **bind** specific **DNA** sequences, resulting in enhanced transcription of responsive genes. The neuroprotective effects of CNTF have been demonstrated in a number of in vitro cell models as well as in vivo in mutant mouse strains which exhibit motor neuron degeneration. Intracerebral administration of CNTF and CNTF analogs has also been shown to protect striatal output neurons in rodent and primate models of Huntington's disease. Treatment of humans and animals with CNTF is also known to **induce** weight loss characterized by a preferential loss of body fat. When administered systemically, CNTF activates downstream signaling molecules such as STAT-3 in areas of the hypothalamus which **regulate** food intake. In addition to its neuronal actions, CNTF and analogs have been shown to act on non-neuronal cells such as glia, hepatocytes, skeletal muscle, embryonic stem cells and bone marrow stromal cells. Copyright (C) 2000 Elsevier Science B.V.

L15 ANSWER 3 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 2

TI Chlorophyllin suppression of lipopolysaccharide-induced nitric oxide production in RAW 264.7 cells.

SO Toxicology and Applied Pharmacology, (July 15, 2000) Vol. 166, No. 2, pp. 120-127. print.
ISSN: 0041-008X.

AU Cho, Kyung-Joo; Han, Seung Hyun; Kim, Bu Yeo; Hwang, Seong-Gu; Park, Kwang-Kyun; Yang, Kyu-Hwan; Chung, An-Sik (1)

AB Chlorophyllin (CHL), a water-soluble derivative of chlorophyll, functions as an anticarcinogen and antioxidant. In the present study, we investigated the effect of CHL on nitric oxide production in lipopolysaccharide (LPS)-stimulated RAW 264.7 cells. Treatment with CHL inhibited nitric oxide production in the LPS-stimulated RAW 264.7 cells in a dose-related manner. Competitive RT-PCR analysis, using a DNA competitor as an internal standard, demonstrated that the treatment with 1, 10, and 50 muM CHL decreased LPS-**induced** iNOS mRNA expression in a concentration-dependent manner. Since the expression of the iNOS gene is mainly **regulated** by NF-kappaB, we then examined the effects of CHL on the NF-kappaB **DNA binding** activity, using an electrophoretic mobility shift assay. CHL down-**regulated** the NF-kappaB **DNA binding** on its cognate recognition site at the concentrations just noted. Employing a transfection and reporter **gene expression system** with p(NF-kappaB)3-chloramphenicol acetyl transferase (CAT), the treatment of CHL produced a dose-dependent inhibition of CAT activity in RAW 264.7 cells. Furthermore, CHL partially restored LPS-decreased IkappaBalpha, an inhibitory protein against NF-kappaB activation, in the cytosolic extract from the LPS-treated cells determined by immunoblot analysis. CHL also protected the hydroxyl radical-**induced** cytotoxicity in RAW 264.7 cells, indicating its antioxidant effect. These results suggest that CHL suppresses the nitric oxide production and iNOS mRNA expression mediated by the inhibition of NF-kappaB activation, and its action mechanism may be based on its antioxidant effect.

L15 ANSWER 4 OF 30 TOXLINE DUPLICATE 3

TI AFLATOXIN CONTROL THROUGH TARGETING GENE CLUSTER GOVERNING AFLATOXIN SYNTHESIS IN CORN & COTTONSEE.

SO (1999). FEDRIP DATABASE, NATIONAL TECHNICAL INFORMATION SERVICE (NTIS).

AU BHATNAGAR D; WRIGHT M S; EHRLICH K

AB RPROJ/FEDRIP OBJECTIVE: Develop strategies to eliminate aflatoxin contamination of corn and cottonseed based on understanding and manipulating the expression of genes located in a gene cluster which governs aflatoxin production by Aspergillus flavus group fungi.

APPROACH:

Map, sequence and study transcriptional **regulation** of genes located within aflatoxin gene cluster. Identify **DNA binding** proteins/chemical modulators that influence **regulation** of aflatoxin production. Based on knowledge of molecular **regulation**, determine feasibility of selectively inhibiting aflatoxin gene expression. Selectively inactivate genes in cluster through gene disruption techniques. Determine effects of individual gene disruptions on aflatoxin biosynthesis, infectivity of disrupted strain in plants and other morphological or phenotypic effects of gene disruption in the strain. Using pertinent genes/probes identified, determine the molecular basis for the phenomenon of natural non-production in certain members of the A. flavus group. Monitor aflatoxin gene expression in A. flavus-infected plant tissues through use of aflatoxin gene promoter-reporter gene fusions. -- PROGRESS: Further efforts to characterize the Aspergillus parasiticus aflatoxin gene cluster has led to the identification of two additional genes, adhA and aflJ. The predicted ADHA protein belongs to the family of short-chain alcohol dehydrogenases, and probably carries out a reductive reaction similar to the function of the already identified nor-1 and ver-1 gene products. The aflJ gene, although containing no known structural motifs, together with the aflatoxin **regulatory** gene aflR, elevates the production of aflatoxin and its precursors in the transformants. Toassess the effect of environmental factors on aflatoxin production, several A. parasiticus transformants were prepared with reporter genes (uidA and GUS) linked to the promoters of key aflatoxin pathway enzyme genes (pksA, avnA, omt-1, and aflR) as member strains for this study of toxin production in culture or in crops. Preliminary results with these fungal transformants suggest that several known aflatoxin inhibitors do notaffect gene transcription, but rather may alter precursor utilization.The expression of GUS under control of these promoters was measured under aflatoxin **inducing** and non-**inducing** conditions, as well as during growth of the fungus in the presence of a number of cotton and corn volatile compounds. A fungal **gene expression system** based on the green fluorescent protein (GFP) reporter gene has also been developed to study the extent and route of invasion of this fungus in both cotton and corn.

L15 ANSWER 5 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 4

TI Overexpression of RelA causes G1 arrest and apoptosis in a pro-B cell line.

SO Journal of Biological Chemistry, (March 26, 1999) Vol. 274, No. 13, pp. 8708-8716.
ISSN: 0021-9258.

AU Sheehy, Ann M.; Schlissel, Mark S. (1)

AB NF-kappaB/Rel family proteins form a network of posttranslationally **regulated** transcription factors that respond to a variety of extracellular stimuli and mediate distinct cellular responses. These responses include cytokine gene expression, **regulated** cell cycle activation, and both the protection from and **induction** of the cell death program. To examine the function of individual Rel family proteins in B cell development and resolve their role in the signaling of

apoptosis, we used a tetracycline-**regulated gene expression system** to overexpress either c-Rel or RelA in the transformed [redacted]-B cell line 220-8. Elevated l[redacted]els of RelA, but not c-Rel, **induced** a G1 cell cycle arrest followed by apoptosis. Both the **DNA binding** and transactivation domains of RelA were required for this effect. When RelA was overexpressed in the immature B cell line WEHI 231 or the mature B cell line M12, neither cell cycle arrest nor apoptosis was evident. The differential effects of elevated RelA levels in these cell lines suggests that susceptibility to NF-kappaB-**induced** apoptosis may reflect a relevant selection event during B cell development.

L15 ANSWER 6 OF 30 LIFESCI COPYRIGHT 2000 CSA
TI Tet B or not tet B: Advances in tetracycline- inducible gene expression
SO Proceedings of the National Academy of Sciences, USA [Proc. Natl. Acad. Sci. USA], (19990202) vol. 96, no. 03, pp. 797-799.
ISSN: 0027-8424.
AU Blau, H.M.; Rossi, F.M.V.
AB Be it the B class, or another class of tetracycline (tet) repressor, the utility and specificity of transcriptional **regulators** based on this family of prokaryotic **DNA binding** proteins is unparalleled. A method for **regulating** gene expression at will in mammalian cells has long been the holy grail. Transfections of uncontrolled numbers of plasmids and unregulated gene expression were breakthroughs in the early days of molecular biology when genes encoding abundant proteins first were introduced into cultured cells. Gone are those days and those antiquated and limited methods. Fine tuning is now essential. We need **systems** in which **gene expression** can be repressed and then **induced** at will. Such control is essential for products that are growth inhibitory or toxic, for example, components of the apoptotic cascade. We need to be able to monitor different levels of gene expression during discrete time periods in cultured cells and in animals to understand the **regulation** of signal transduction that culminates in different cell fates. Cells that stably express deleterious proteins or cytokines may be lost or their phenotype altered during long-term selection. Clearly, for gene therapy, **regulation** is crucial. Modulating gene expression in cycles that mimic endogenous patterns is highly desirable, and avoiding toxic levels is a must.

L15 ANSWER 7 OF 30 AGRICOLA DUPLICATE 5
TI Transcriptional activator TGV mediates dexamethasone-inducible and tetracycline-inactivatable gene expression.
SO The Plant journal : for cell and molecular biology, July 1999. Vol. 19, No. 1. p. 87-95
Publisher: Oxford : Blackwell Sciences Ltd.
ISSN: 0960-7412
AU Bohner, S.; Lenk, I.; Rieping, M.; Herold, M.; Gatz, C.
AB A chemically **regulated gene expression system** that can be switched on with dexamethasone and switched off with tetracycline was constructed. It is based on a transcriptional activator (TGV) that consists of the Tn10 encoded Tet repressor, the rat glucocorticoid receptor hormone binding domain and the transcriptional activation domain of Herpes simplex virion protein VP16. When stably expressed in transgenic tobacco plants, it mediates dexamethasone-**inducible** transcription from a synthetic promoter (P(Top10)) consisting of seven tet operators upstream of a TATA-box. Tetracycline interferes with **induction** by negatively **regulating** the **DNA-binding** activity of the TetR moiety of TGV. The boundaries of the expression window of the TGV-driven P(Top10) reach from undetectable levels of the reporter enzyme beta-glucuronidase in the absence of dexamethasone to **induced** levels reaching 15-20% of the Cauliflower Mosaic Virus 35S promoter (P(CaMV35S)). By modifying the sequence of P(Top10), we generated a new target promoter (P(tax)) that is stably expressed over several generations and that can be activated to

levels comparable to P(CaMV35S), while yielding only slightly elevated background activities.

L15 ANSWER 8 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 6
TI Transcriptional activator TGV mediates dexamethasone-inducible and tetracycline-inactivatable gene expression.
SO Plant Journal, (July, 1999) Vol. 19, No. 1, pp. 87-95.
ISSN: 0960-7412.
AU Boehner, Steffen; Lenk, Ingo; Rieping, Mechthild; Herold, Michael; Gatz, Christiane (1)
AB A chemically **regulated gene expression system** that can be switched on with dexamethasone and switched off with tetracycline was constructed. It is based on a transcriptional activator (TGV) that consists of the Tn10 encoded Tet repressor, the rat glucocorticoid receptor hormone binding domain and the transcriptional activation domain of Herpes simplex virion protein VP16. When stably expressed in transgenic tobacco plants, it mediates dexamethasone-**inducible** transcription from a synthetic promoter (PTop10) consisting of seven tet operators upstream of a TATA-box. Tetracycline interferes with **induction** by negatively **regulating** the **DNA-binding** activity of the TetR moiety of TGV. The boundaries of the expression window of the TGV-driven PTop10 reach from undetectable levels of the reporter enzyme beta-glucuronidase in the absence of dexamethasone to **induced** levels reaching 15-20% of the Cauliflower Mosaic Virus 35S promoter (PCaMV35S). By modifying the sequence of PTop10, we generated a new target promoter (PTax) that is stably expressed over several generations and that can be activated to levels comparable to PCaMV35S, while yielding only slightly elevated background activities.

L15 ANSWER 9 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 7
TI Suppression of the interleukin-2 gene expression by aflatoxin B1 is mediated through the down-regulation of the NF-AT and AP-1 transcription factors.
SO Toxicology Letters (Shannon), (July 30, 1999) Vol. 108, No. 1, pp. 1-10.
ISSN: 0378-4274.
AU Han, Seung Hyun; Jeon, Young Jin; Yea, Sung Su; Yang, Kyu-Hwan (1)
AB The effect of aflatoxin B1 (AFB1) on the interleukin-2 (IL-2) gene expression was investigated in thymocytes of B6C3F1 mice, Jurkat E6-1 human T-cell leukemia, and EL4.IL-2 murine thymoma. AFB1 inhibited the phorbol-12-myristate-13-acetate/ionomycin (PMA/Io)-**induced** IL-2 mRNA expression in the murine thymocytes and Jurkat E6-1 cells as determined by qualitative RT-PCR, while no effect was observed in the EL4.IL-2 cells. Electrophoretic mobility shift assay indicated that AFB1 treatment showed an inhibition of the NF-AT and AP-1 **DNA binding** in PMA/Io-stimulated thymocytes and Jurkat E6-1 cells. No effect was observed on the Oct and NF-kappaB **DNA binding** . Employing a reporter **gene expression system** with p(NF-AT)3-CAT and p(AP-1)3-CAT, treatment with AFB1 to the transfected Jurkat E6-1 cells also showed an inhibition of the PMA/Io-**induced** NF-AT/CAT and AP-1/CAT activities. These results suggest that suppression of the IL-2 gene expression by AFB1 is mediated through the down-**regulation** of the NF-AT and AP-1 activation.

L15 ANSWER 10 OF 30 TOXLINE
TI TOXICOLOGICAL CONTROL MECHANISMS OF HUMAN CYP1A2 GENE.
SO (1998). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
AU QUATTROCHI L C
AB RPROJ/CRISP Toxicity of the chemical class of xenobiotics that include polycyclic aromatic hydrocarbons (PAH) and halogenated hydrocarbons, such as polychlorinated biphenyls and dibenzodioxins, most likely occurs through control of gene expression. The molecular mechanism is largely unknown, but is currently believed to involve, In part, a cytosolic receptor, the aryl hydrocarbon or Ah-receptor. If the mechanism

responsible for the many toxic effects associated with these classes of chemicals is to be unraveled, it will be necessary to study other genes that may be **regulated** through additional cellular mediators. This grant proposal focuses on the human cytochrome P4501A2 gene (CYP1A2), a member of the PAH-**inducible** CYP1A gene family that is prominent in human liver, and metabolizes drugs, such as acetaminophen, caffeine, environmental agents such as arylamines and dietary constituents, such as heterocyclic amines and aflatoxins. The molecular mechanism for the **regulation** of the human CYP1A2 gene will be studied through the characterization of cis-acting elements and identification of trans-acting factors utilizing transient transfection assays and in vitro **DNA binding** assays, such as DNase I footprinting. In vivo footprinting studies in human primary hepatocytes will be conducted to examine the temporal relationship among transcription factors in **regulating** CYP1A2 **gene expression**. Several model **systems** will be utilized for the proposed research, including human hepatoma cell lines, human liver and non-proliferating cultures of human hepatocytes. A Cell Culture Core and Human Tissue Bank will provide the necessary support for these studies. It is believed that a combination of these molecular and cell culture approaches will elucidate the mechanism by which this important gene is **regulated**.

L15 ANSWER 11 OF 30 BIOTECHDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Two novel adenovirus vector systems permitting regulated protein expression in gene transfer experiments;
adeno virus vector production, used for gene transfer, and regulation of recombinant protein induction in gene therapy
SO J.Virol.; (1998) 72, 10, 8358-61
CODEN: JOVIAM ISSN: 0022-538X
AU Molin M; Shoshan M C; Ohman-Forslund K; Linder S; *Akusjarvi G
AN 1999-11555 BIOTECHDS
AB Two adeno virus vector systems based on the tetracycline-**regulated** Tet-ON- and the RU 486-**regulated** progesterone-antagonist-**induced gene expression systems** were produced. The Tet-ON system, designated AdCMVrtTA, consisted of the reverse tetracycline repressor protein fused to herpes simplex virus VP16 transcriptionally active domain linked to the cytomegalo virus (CMV) promoter, and inserted into adeno virus type 5 (Ad5). In the Ru 486-**regulated** system, designated AdCMVProg, a chimeric transactivator protein consisting of hPRB891 ligand **binding** domain and Gal4 **DNA binding** domain, and HSV VP16 transactivator domain were linked to a CMV promoter and inserted into Ad5 dl309. Both systems allowed tight control of chloramphenicol-acetyltransferase (EC-2.3.1.28) reporter gene expression in a variety of cells. The Tet-ON system **induced** approximately 1,800-fold and the RU-486-**regulated** system **induced** about 600-fold levels of gene expression. Reporter gene expression could be adjusted over a wide range, by varying the concentration of the **inducer**. The Tet-ON system could also be used for efficient control of gene expression in mice. (15 ref)

L15 ANSWER 12 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 8
TI Transforming growth factor-beta 1 (TGF-beta1) promotes IL-2 mRNA expression through the up-regulation of NF-kappaB, AP-1 and NF-AT in EL4 cells.
SO Journal of Pharmacology and Experimental Therapeutics, (Dec., 1998) Vol. 287, No. 3, pp. 1105-1112.
ISSN: 0022-3565.
AU Han, Seung H.; Yea, Sung Su; Jeon, Young J.; Yang, Kyu-H.; Kaminski, Norbert E. (1)
AB Transforming growth factor beta1 (TGF-beta1) has been previously shown to

modulate interleukin 2 (IL-2) secretion by activated T-cells. In the present studies, we determined that TGF-beta1 **induced** IL-2 mRNA expression in th[redacted]urine T-cell line EL4, in the [redacted]sence of other stimuli.

IL-2 mRNA expression was significantly **induced** by TGF-beta1 (0.1-1 ng/ml) over a relatively narrow concentration range, which led to the **induction** of IL-2 secretion. Under identical condition, we examined the effect of TGF-beta1 on the activity of nuclear factor AT (NF-AT), nuclear factor kappaB (NF-kappaB), activator protein-1 (AP-1) and

octamer, all of which contribute to the **regulation** of IL-2 gene expression. Electrophoretic mobility shift assays showed that TGF-beta1 markedly increased NF-AT, NF-kappaB and AP-1 binding to their respective cognate **DNA binding** sites, whereas octamer binding remained constant, as compared with untreated cells. Employing a reporter **gene expression system** with p(NF-kappaB)3CAT, p(NF-AT)3-CAT and p(AP-1)3-CAT, TGF-beta1 treatment of transfected EL4 cells **induced** a dose-related increase in chloramphenicol acetyltransferase activity that correlated well with the **DNA binding** profile found in the electrophoretic mobility shift assay studies. These results show that TGF-beta1, in the absence of any additional stimuli, up-**regulates** the activity of key transcription factors involved in IL-2 gene expression, including NF-AT, NF-kappaB and AP-1, to help promote IL-2 mRNA expression by EL4 cells.

L15 ANSWER 13 OF 30 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.DUPLICATE 9
TI Transforming growth factor-beta 1 (TGF-.beta.1) promotes IL-2 mRNA expression through the up-regulation of NF-.kappa.B, AP-1 and NF-AT in EL4 cells.
SO Journal of Pharmacology and Experimental Therapeutics, (1998) 286/3 (1105-1112).
Refs: 35
ISSN: 0022-3565 CODEN: JPETAB
AU Han S.H.; Sung Su Yea; Jeon Y.J.; Yang K.-H.; Kaminski N.E.
AB Transforming growth factor .beta.1 (TGF-.beta.1) has been previously shown to modulate interleukin 2 (IL-2) secretion by activated T-cells. In the present studies, we determined that TGF-.beta.1 **induced** IL-2 mRNA expression in the murine T-cell line EL4, in the absence of other stimuli. IL-2 mRNA expression was significantly **induced** by TGF-.beta.1 (0.1-1 ng/ml) over a relatively narrow concentration range, which led to the **induction** of IL-2 secretion. Under identical condition, we examined the effect of TGF-.beta.1 on the activity of nuclear factor AT (NF-AT), nuclear factor .kappa.B (NF-.kappa.B), activator protein-1 (AP-1) and octamer, all of which contribute to the **regulation** of IL-2 gene expression. Electrophoretic mobility shift assays showed that TGF-.beta.1 markedly increased NF-AT, NF-.kappa.B and AP-1 binding to their respective cognate **DNA binding** sites, whereas octamer binding remained constant, as compared with untreated cells. Employing a reporter **gene expression system** with p(NF- .kappa.B)3-CAT, p(NF-AT)3-CAT and p(AP-1)3-CAT, TGF-.beta.1 treatment of transfected EL4 cells **induced** a dose-related increase in chloramphenicol acetyltransferase activity that correlated well with the **DNA binding** profile found in the electrophoretic mobility shift assay studies. These results show that TGF-.beta.1, in the absence of any additional stimuli, up-**regulates** the activity of key transcription factors involved in IL-2 gene expression, including NF-AT, NF-.kappa.B and AP-1, to help promote IL-2 mRNA expression by EL4 cells.

L15 ANSWER 14 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 10
TI Suppression of interleukin-2 by the putative endogenous cannabinoid 2-arachidonyl-glycerol is mediated through down-regulation of the nuclear factor of activated T cells.

SO Molecular Pharmacology, (April, 1998) Vol. 53, No. 4, pp. 676-683. ISSN: 0026-895X.

AU Ouyang, Yanli; H[redacted]g, Seong Gu; Han, Seung Hyun; [redacted]inski, Norbert E. (1)

AB 2-Arachidonyl-glycerol (2-Ara-Gl) recently was identified as a putative endogenous ligand for cannabinoid receptor types CB1 and CB2 by competitive binding. More recent immune function assays demonstrated that 2-Ara-Gl possessed immunomodulatory activity. Because several plant-derived cannabinoids inhibit interleukin-2 (IL-2) expression, 2-Ara-Gl was investigated for its ability to modulate this cytokine. The direct addition of 2-Ara-Gl to mouse splenocyte cultures suppressed phorbol-12-myristate-13-acetate plus ionomycin-**induced** IL-2 secretion and steady state mRNA expression in a dose-dependent manner. 2-Ara-Gl also produced a marked inhibition of IL-2 promotor activity as determined by transient transfection of EL4.IL-2 cells with a pl L-2-CAT construct. 2-Ara-Gl at 5, 10, 20, and 50 muM suppressed phorbol-12-myristate-13-acetate plus ionomycin-**induced** IL-2 promotor activity by 18%, 28%, 39%, and 54%, respectively. To further characterize the mechanism for the transcriptional **regulation** of IL-2 by 2-Ara-Gl, the **DNA-binding** activity of transcription factors, nuclear factor of activated T cells (NF-AT), nuclear factor for immunoglobulin K chain in B cells (NF-kappaB/Rel), activator protein-1 (AP-1), octamer, and cAMP-response element binding protein was evaluated by electrophoretic mobility shift assay in mouse splenocytes. In addition, a reporter **gene expression system** for p(NF-kappaB),CAT, p(NF-AT)3-CAT, and p(AP-1)3-CAT was used in transiently transfected EL4.IL-2 cells to determine the effect of 2-Ara-Gl on promoter activity for each of the specific transcription factors. 2-Ara-Gl reduced both the NF-AT-binding and promoter activity in a dose-dependent manner and, to a lesser degree, NFkappaB/Rel-binding and promoter activity. No significant effect was observed on octamer- and cAMP-response element-**binding** activity. AP-1 **DNA-binding** activity was not inhibited by 2-AraGl, but a modest inhibition of promoter activity was observed.

L15 ANSWER 15 OF 30 TOXLINE

TI TOXICOLOGICAL CONTROL MECHANISMS OF HUMAN CYP1A2 GENE.

SO (1997). Crisp Data Base National Institutes Of Health. Award Type: G = Grant

AU QUATTROCHI L C

AB RPROJ/CRISP Toxicity of the chemical class of xenobiotics that include polycyclic aromatic hydrocarbons (PAH) and halogenated hydrocarbons, such as polychlorinated biphenyls and dibenzodioxins, most likely occurs through control of gene expression. The molecular mechanism is largely unknown, but is currently believed to involve, In part, a cytosolic receptor, the aryl hydrocarbon or Ah-receptor. If the mechanism responsible for the many toxic effects associated with these classes of chemicals is to be unraveled, it will be necessary to study other genes that may be **regulated** through additional cellular mediators. This grant proposal focuses on the human cytochrome P4501A2 gene (CYP1A2), a member of the PAH-**inducible** CYP1A gene family that is prominent in human liver, and metabolizes drugs, such as acetaminophen, caffeine, environmental agents such as arylamines and dietary constituents, such as heterocyclic amines and aflatoxins. The molecular mechanism for the **regulation** of the human CYP1A2 gene will be studied through the characterization of cis-acting elements and identification of trans-acting factors utilizing transient transfection assays and in vitro **DNA binding** assays, such as DNase I footprinting. In vivo footprinting studies in human primary hepatocytes will be conducted to examine the temporal relationship among transcription factors in **regulating** CYP1A2 **gene expression** . Several model **systems** will be utilized for the proposed research, including human hepatoma cell lines, human liver and non-proliferating cultures of human hepatocytes. A Cell Culture Core and

Human Tissue Bank will provide the necessary support for these studies. It is believed that [redacted] combination of these molecular [redacted]d cell culture approaches will elucidate the mechanism by which this important gene is **regulated**.

L15 ANSWER 16 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 11
TI Chronic Fos-related antigens: Stable variants of DELTA-FosB induced in brain by chronic treatments.
SO Journal of Neuroscience, (1997) Vol. 17, No. 13, pp. 4933-4941. ISSN: 0270-6474.
AU Chen, Jingshan; Kelz, Max B.; Hope, Bruce T.; Nakabeppu, Yusaku; Neslter, Eric J. (1)
AB Fos family transcription factors are believed to play an important role in the transcriptional responses of the brain to a variety of stimuli. Previous studies have described 35 and 37 kDa Fos-like proteins, termed chronic Fos-related antigens (FRAs), that are **induced** in brain in a region-specific manner in response to several chronic perturbations, including chronic electroconvulsive seizures, psychotropic drug treatments, and lesions. We show in this study that the chronic FRAs are isoforms of DELTA-FosB, a truncated splice variant of FosB that accumulate in brain after chronic treatments because of their stability. DELTA-FosB cDNA encodes the expression of 33, 35, and 37 kDa proteins that arise from a single AUG translation start site. The 35 and 37 kDa proteins correspond to the chronic FRAs that are **induced** in brain by chronic treatments, whereas the 33 kDa protein corresponds to a Fos-like protein that is **induced** in brain by acute treatments, findings based on migration on one- and two-dimensional Western blots with anti-FRA and anti-FosB antibodies. Using cells in which DELTA-FosB or FosB expression is under the control of a tetracycline-**regulated gene expression system**, we show that the 37 kDa DELTA-FosB protein exhibits a remarkably long half-life, the 35 kDa DELTA-FosB protein exhibits an intermediate half-life, and the 33 kDa DELTA-FosB protein and all FosB-derived proteins exhibit relatively short half-lives. Moreover, we show that the 33 kDa DELTA-FosB protein is the first to appear after activation of DELTA-FosB expression. Finally, DELTA-FosB proteins are shown to possess **DNA-binding** activity and to exert potent transactivating effects in reporter gene assays. Together, these findings support a scheme wherein DELTA-FosB, expressed as a 33 kDa protein, is modified to form highly stable isoforms of 35 and 37 kDa. As a result, these stable isoforms gradually accumulate in the brain with repeated treatments to mediate forms of long-lasting neural and behavioral plasticity.

L15 ANSWER 17 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 12
TI Inhibition of bovine endothelial cell activation in vitro regulated expression of a transdominant inhibitor of NF-kappa-B.
SO Journal of Clinical Investigation, (1997) Vol. 99, No. 4, pp. 763-772. ISSN: 0021-9738.
AU Anrather, Josef; Csizmadia, Vilmos; Brostjan, Christine; Soares, Miguel P.; Bach, Fritz H.; Winkler, Hans (1)
AB The activation of endothelial cells is a recurrent phenomenon linked to pathologic conditions such as inflammation, chronic arthritis, allo- and xenograft rejection. To inhibit endothelial cell activation we have constructed a transactivation-deficient derivative of the p65/RelA subunit of NF-kappa-B, a transcription factor known to be crucial for the

induction of adhesion molecules, cytokines and procoagulants in activated endothelial cells. This protein (p65RHD) comprises the Rel homology domain of the RelA subunit, retaining dimerization, **DNA binding**, and nuclear localization functions, but is deficient in transcriptional activation, and acts as a competitive inhibitor of NF-kappa-B. Our data demonstrate that p65RHD is a potent and specific inhibitor of NF-kappa-B-mediated **induction** of a number of genes, such as I-kappa-B-alpha, IL-8, E-selectin, P-selectin, and tissue factor in endothelial cells. Furthermore, tetracycline-**inducible** expression of p65RHD in stably transfected primary endothelial cells inhibits the **induction** of gene expression equally well. This **regulated system** of **gene expression** provides the basis for a novel therapeutic approach to the pathologic effects of endothelial cell activation, especially in delayed xenograft rejection, by using transgenic animals as organ donors.

L15 ANSWER 18 OF 30 AGRICOLA DUPLICATE 13
TI Controls of the expression of aspA, the aspartyl protease gene from Penicillium roqueforti.
SO Molecular & general genetics : MGG, Nov 1997. Vol. 256, No. 5. p. 557-565
Publisher: Berlin, Germany : Springer-Verlag Berlin.
CODEN: MGGEAE; ISSN: 0026-8925
AU Gente, S.; Durand-Poussereau, N.; Fevre, M.
AB The gene (aspA) encoding the extracellular aspartyl protease from Penicillium roqueforti was cloned and characterized. Northern hybridization analyses and beta-casein degradation assays revealed that aspA was strongly **induced** by casein in the medium and efficiently repressed by ammonia. External alkaline pH overrides casein **induction**, resulting in aspA repression. Cis-acting motifs known to mediate nitrogen and pH **regulation** of fungal gene expression are present in the aspA promoter and protein-**DNA binding** experiments showed that mycelial proteins interact with various regions of the promoter. Due to the efficient environmental controls on aspA expression, the promoter of aspA is an attractive candidate for the development of a controllable **gene expression system** in P. roqueforti.

L15 ANSWER 19 OF 30 TOXLINE
TI TOXICOLOGICAL CONTROL MECHANISMS OF HUMAN CYP1A2 GENE.
SO (1996). Crisp Data Base National Institutes Of Health. Award Type: G = Grant
AU QUATTROCHI L C
AB RPROJ/CRISP Toxicity of the chemical class of xenobiotics that include polycyclic aromatic hydrocarbons (PAH) and halogenated hydrocarbons, such as polychlorinated biphenyls and dibenzodioxins, most likely occurs through control of gene expression. The molecular mechanism is largely unknown, but is currently believed to involve, In part, a cytosolic receptor, the aryl hydrocarbon or Ah-receptor. If the mechanism responsible for the many toxic effects associated with these classes of chemicals is to be unraveled, it will be necessary to study other genes that may be **regulated** through additional cellular mediators. This grant proposal focuses on the human cytochrome P4501A2 gene (CYP1A2), a member of the PAH-**inducible** CYP1A gene family that is prominent in human liver, and metabolizes drugs, such as acetaminophen, caffeine, environmental agents such as arylamines and dietary constituents, such as heterocyclic amines and aflatoxins. The molecular mechanism for the **regulation** of the human CYP1A2 gene will be studied through the characterization of cis-acting elements and identification of trans-acting factors utilizing transient transfection assays and in vitro **DNA binding** assays, such as DNase I footprinting. In vivo footprinting studies in human primary hepatocytes will be conducted to examine the temporal relationship among transcription

factors in **regulating** CYP1A2 **gene expression**
. Several model **systems** will be utilized for the proposed
research, including human hepatoma cell lines, human liver and
non-proliferating cultures of human hepatocytes. A Cell Culture Core and
Human Tissue Bank will provide the necessary support for these studies.
It
is believed that a combination of these molecular and cell culture
approaches will elucidate the mechanism by which this important gene is
regulated.

L15 ANSWER 20 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 14
TI Activation of a nuclear DNA-binding protein recognized by a
transcriptional element, bcn-1, from the laminin B2 chain gene promoter.
SO Journal of Biological Chemistry, (1996) Vol. 271, No. 31, pp.
18981-18988.
ISSN: 0021-9258.
AU Suzuki, Hideaki; O'Neill, Bruce C.; Suzuki, Yu; Denisenko, Oleg N.;
Bomsztyk, Karol (1)
AB Treatment of mesangial cells with either phorbol 12-myristate 13-acetate
(PMA) or interleukin-1-beta **induces** an increase in laminin B2
chain mRNA levels. In other **systems**, activation of **gene**
expression by these agents is transcriptionally mediated. To
identify transcription factors that control expression of laminin B2
chain
gene, we employed a strategy consisting of a computer-based analysis of
murine and human gene promoter sequences and gel shift assays. Although
overall the laminin B2 chain promoters from the two species have low
sequence similarity, the mouse promoter contained sequences that were
also
contained in one motif, 5'-CCCCGCCCACCTCGCGCGC-3', designated bcn-1, from
the human promoter. Treatment of mesangial cells with either PMA or
interleukin-1-beta **induced** a transient increase in nuclear
DNA binding activity, designated BCN-1, recognized the
bcn-1 motif in a gel shift assay. A single nucleotide replacement in the
bcn-1 motif abolished **DNA binding**, indicating that
bcn-1-BCN-1 complex formation is highly specific. In transient
transfections, the ability of PMA to **induce** the laminin B2 chain
promoter was abolished by mutating the bcn-1 motif. These results suggest
that the bcn-1 element and its cognate **inducible** BCN-1 protein
regulate laminin B2 chain gene transcription.

L15 ANSWER 21 OF 30 TOXLINE
TI TOXICOLOGICAL CONTROL MECHANISMS OF HUMAN CYP1A2 GENE.
SO (1995). Crisp Data Base National Institutes Of Health. Award Type: G =
Grant
AU QUATTROCHI L C
AB RPROJ/CRISP Toxicity of the chemical class of xenobiotics that include
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I footprinting. In vivo footprinting studies in human primary hepatocytes will be conducted to examine the temporal relationship among transcription factors in **regulating** CYP1A2 **gene expression**. Several model **systems** will be utilized for the proposed research, including human hepatoma cell lines, human liver and non-proliferating cultures of human hepatocytes. A Cell Culture Core and Human Tissue Bank will provide the necessary support for these studies. It is believed that a combination of these molecular and cell culture approaches will elucidate the mechanism by which this important gene is **regulated**.

L15 ANSWER 22 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 15
TI Improved gene expression in Aspergillus nidulans.
SO Canadian Journal of Botany, (1995) Vol. 73, No. SUPPL. 1 SECT. E-H, pp. S876-S884.
ISSN: 0008-4026.
AU Hintz, William E. (1); Kalsner, Inge; Plawinski, Ewa; Guo, Zimin; Lagosky, Peter A.
AB A variety of **gene expression systems** have been developed that utilize the promoter and transcriptional **regulatory** sequences derived from carbon-catabolite repressed genes for the expression of heterologous **genes**. The alcA **expression system** of Aspergillus nidulans utilizes the promoter and **regulatory** sequences derived from the alcohol dehydrogenase I (alcA) gene. Expression of the alcA gene is repressed by a **DNA-binding** protein (CreA) in the presence of glucose and **induced** by ethanol under glucose-depleted conditions. One problem encountered during the expression of therapeutic proteins in A. nidulans is the coexpression of secreted proteases at the time of maximal secretion of heterologous product. To avoid the proteases we created an alcA promoter variant that is no longer sensitive to glucose repression hence could drive expression at earlier time points during the fermentation. The use of this promoter variant in the expression of recombinant interleukin-6 is discussed. A second problem encountered during the expression of high-quality human therapeutic proteins in Aspergillus is aberrant glycosylation. Lower eukaryotic systems, such as Aspergillus, tend to add highly branched mannosidic chains to heterologous secreted protein products. N-Glycans can be important for both the structure and function of specific glycoproteins, hence efforts are being made to in vivo alter the type and complexity of N-glycans substituted by A. nidulans.

L15 ANSWER 23 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 16
TI Second messenger-mediated transcriptional regulation of neural genes and possible drug action sites.
SO Folia Pharmacologica Japonica, (1995) Vol. 106, No. 6, pp. 365-378.
ISSN: 0015-5691.
AU Higuchi, Hiroshi; Li, Bing-Sheng
AB Second messenger systems **regulate** transcription initiation of immediate-early genes (IEFs) through phosphorylation of transcriptional factors and repressors. Tissue-specific late response genes (LRGs) are **induced** dependently on protein synthesis slowly after IEGs, but the mechanisms of **regulation** of LRGs are still unknown. In this review, the mechanisms of transcriptional **regulation** of IEGs are summarized and possible drug action sites are discussed. As to the neuropeptide Y (NPY) gene, a typical neuronal LRG, the approach was introduced to elucidate the transcriptional **regulations** of the NPY gene **induced** by membrane depolarization and NGF-**induced** neuronal differentiation. The second messenger systems were Ca/calmodulin dependent protein kinases (CaM) and NGF-**induced**

MAP kinases, respectively. The unique CaM- and NGF-responsive elements and
DNA-binding fact[redacted] were identified. The NDF1 pro[redacted]n bound to NGF-RE were cloned and characterized. NDF1 seems to a novel transcriptional factor that **regulates** neurotrophin-**induced** transcription of LRGs. Thus identification of novel **regulatory** factors is required to elucidate mechanisms of gene expression including transcriptional initiation, and pharmacological studies are also necessary to discover the novel drug action sites in the **gene expression system**.

L15 ANSWER 24 OF 30 BIOTECHDS COPYRIGHT 2000 DERWENT INFORMATION LTD
TI A regulatory system for use in gene transfer; human progesterone receptor deletion mutant chimeric regulator construction for target gene transfer and transcription control (conference abstract)
SO J.Cell.Biochem.; (1995) Suppl.21A, 355
CODEN: JCEBD5 ISSN: 0730-2312
Keystone Symposium, 24th Annual Meeting, Gene Therapy and Molecular Medicine, Steamboat Springs, CO, March 26-April 1, 1995.
AU O'Malley B W; Wang Y; Tsai S Y
AN 1996-03906 BIOTECHDS
AB The C-terminal deletion mutant of the human progesterone receptor (hPRB891) does not bind progesterone, but can bind RU486 and other progesterone-antagonists. A chimeric **regulator** (plasmid pGL-VP) was constructed by fusing the ligand-binding domain of hPRB891 to the yeast transcriptional activator GAL4 ***DNA*** **-binding** domain and the herpes simplex virus protein VP16 activation domain. The chimeric **regulator** activates target genes containing the GAL4-binding sites in transient transfection assays in response to RU486.
This **regulatory** system was validated by ex vivo transplantation of a stable cell line containing the **regulator** and a reporter gene into rats. The RU486 dosage was significantly lower than that required for antagonizing progesterone action. A second generation of vectors was constructed which allowed greater versatility relative to basal levels and **induction** ratios of target gene **expression**. The **gene**-switch **system** represents a **regulatory** system which could be applicable in gene transfer studies involving animals, as well as humans, in which the delivered gene can be specifically turned on/off in response to an exogenous compound. (0 ref)

L15 ANSWER 25 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 17
TI ANALYSIS OF CONSTITUTIVE AND NONINDUCIBLE MUTATIONS OF THE PUT3 TRANSCRIPTIONAL ACTIVATOR.
SO MOL CELL BIOL, (1991) 11 (5), 2609-2619.
CODEN: MCEBD4. ISSN: 0270-7306.
AU MARCZAK J E; BRANDRISS M C
AB The Saccharomyces cerevisiae PUT3 gene encodes a transcriptional activator that **binds** to **DNA** sequences in the promoters of the proline utilization genes and is required for the basal and **induced** expression of the enzymes of this pathway. The sequence of the wild-type PUT3 gene revealed the presence of one large open reading frame capable of encoding a 979-amino-acid protein. The protein contains amino-terminal basic and cysteine-rich domains homologous to the **DNA-binding** motifs of other yeast transcriptional activators. Adjacent to these domains is an acidic domain with a net charge of -17. A second acidic domain with a net charge of -29 is located at the carboxy terminus. The midsection of the PUT3 protein has homology to other activators including GAL4, LAC9, PPR1, and PDR1. Mutations in PUT3 causing aberrant (either constitutive or noninducible) **expression** of target **genes** in this **system** have

been analyzed. One activator-defective and seven activator-constitutive PUT3 alleles have been retrieved from the genome and sequenced to determine the nucleotide changes responsible for the altered function of the protein. The activator-defective mutation is a single nucleotide change within codon 409, replacing glycine with aspartic acid. One activator-constitutive mutation is a nucleotide change at codon 683, substituting phenylalanine for serine. The remaining constitutive mutations resulted in amino acid substitutions or truncations of the protein within the carboxy-terminal 76 codons. Mechanisms for **regulating** the activation function of the PUT3 protein are discussed.

L15 ANSWER 26 OF 30 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 18
TI MAPPING OF FUNCTIONAL AND ANTIGENIC DOMAINS OF THE ALPHA-4 PROTEIN OF HERPES SIMPLEX VIRUS 1.
SO J VIROL, (1988) 62 (2), 454-462.
CODEN: JOVIAM. ISSN: 0022-538X.
AU HUBENTHAL-VOSS J; HOUGHTEN R A; PEREIRA L; ROIZMAN B
AB Monoclonal antibodies to .alpha.4, the major **regulatory** protein of herpes simplex virus 1, have been shown to differ in their effects on the binding of the protein to its **DNA-binding** site in the promoter-**regulatory** domain of an .alpha. gene. To map the epitopes, we expressed truncated **genes** in transient **expression systems**. All 10 monoclonal antibodies tested reacted with the N-terminal 288-amino-acid polypeptide. To map the epitopes more precisely, 29 15-mer oligopeptides, overlapping by five amino acids at each end, were synthesized and reacted with the monoclonal antibodies. The nine reactive monoclonal antibodies were mapped to seven sites. Of the two monoclonal antibodies which blocked the binding of .alpha.4 to DNA, one (H950) reacted with oligopeptide no. 3 near the N terminal of the protein, whereas the second (H942) reacted with oligopeptide no. 23 near the C terminus of the 288-amino acid polypeptide.
In further tests, oligopeptide no. 19 was found to compete with two host proteins, designated as .alpha.H1 and .alpha.H2-.alpha.H3, for **binding** to **DNA** as well as to retard DNA in a band shift assay, whereas oligopeptides no. 26, 27, and 28 enhanced the binding of .alpha.4 to DNA. Moreover, oligopeptide no. 27 was also found to retard DNA in a band shift assay. Polypeptide no. 19 competed with .alpha.4 for **binding** to **DNA**, whereas no. 27 neither enhanced nor competed with the binding of the host polypeptide .alpha.H1 to its binding site in the promoter-**regulatory** domain of an .alpha. gene, but did enhance the binding of the .alpha.H2-.alpha.H3 protein to its binding site. In contrast to these results, the truncated .alpha.4 polypeptide, 825 amino acids long, bound to the viral DNA, whereas a shorter, 519-amino-acid-long, truncated polypeptide did not. The 825-amino-acid polypeptide was previously shown to **induce** in transient expression systems the expression of a late (.gamma.2) viral gene.

L15 ANSWER 27 OF 30 DGENE COPYRIGHT 2000 DERWENT INFORMATION LTD
TI New isolated nucleic acid encoding an insect protein from a Pyrilidae species used for selectively inducing gene expression of a protein of interest in a plant e.g. to regulate plant fertility -
IN Albertsen M C; Brooke C D; Garnaat C W; Roth B A
AB This sequence represents a novel ecdysone receptor (EcR) from the European corn borer. The EcR cDNA was isolated from a European corn borer larval cDNA library, comprising a mixture of cDNA from stage 2, 3, and 4 larvae. Ecdysone controls the timing of development in many insects, coordinating changes in tissue development that results in metamorphosis.
The EcR comprises a ligand-**binding** domain, a **DNA**

binding domain and a transactivation domain. It binds to the steroid hormone 20-hydroxyecdysone (also known as beta-ecdysone) and heterodimerises with a partner molecule, Ultraspiracle (USP; Y87471). The EcR/USP complex binds to ecdysone response elements (EcREs) in the promoters of target genes and transactivates expression of the target genes. EcR and USP are used in **gene expression systems inducible** with ecdysone or ecdysone agonists. In particular, the cell in which the receptor is expressed is a plant cell. The target gene (either native or introduced) in such cells has one or more EcREs engineered into its promoter, enabling expression to be **induced** on treatment with ecdysone or ecdysteroid agonists. Tissue- specific promoters in the EcR/USP expression constructs limit ecdysone **inducibility** to specific tissues or cell types. This permits the compartmentalisation of target gene expression, which may be useful in **regulating** the fertility of transgenic plants. For example, transgenic plants may be generated in which fertility is **inducible** via treatment with ligand, the plant otherwise being sterile. Expression of specific proteins may also be **induced** at specific times in a plant's developmental cycle via use of the expression system. This may be used to **induce** expression of a target gene which enhances the nutritional value of a specific crop, selectively **induces** insecticidal properties or herbicide resistance or heightens plant resistance to environmental factors such as cold or drought

L15 ANSWER 28 OF 30 DGENE COPYRIGHT 2000 DERWENT INFORMATION LTD
TI Tetracycline based regulation of gene expression - uses a tetracycline operator sequence joined to a gene of interest, the gene of interest being induced in the presence, but not absence of the antibiotic
IN Bujard H; Gossen M
AB The present sequence is encoded by a "reverse" Tet repressor (rTetR), which **binds** to its target **DNA** in the presence rather than the absence of tetracycline. The sequence was generated by chemical mutagenesis. rTetR is used in the course of the invention. The specification describes a method for **regulating** expression of a Tet (tetracycline) operator-linked gene in a cell of a subject. The method comprises introducing into the cell a nucleic acid encoding a fusion protein which inhibits transcription in eukaryotic cells, the fusion protein comprising a polypeptide which binds to a Tet operator sequence, operatively linked to heterologous second polypeptide which inhibits transcription in eukaryotic cells and modulating the concentration of a tetracycline (analogue) in the subject. The method is used for the **regulation** of **gene expression system**, using tetracycline (analogues). The system enables a gene coupled to the system to be **induced** in the presence of Tet and then stopped when Tet is removed

L15 ANSWER 29 OF 30 DGENE COPYRIGHT 2000 DERWENT INFORMATION LTD
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inhibits transcription in eukaryotic cells and modulating the concentration of a tetracycline (analogue) in the subject. The method is used for the **re[redacted]lation of gene expression system**, using tetracycline (analogues). The system enables a gene coupled to the system to be **induced** in the presence of Tet and then stopped when Tet is removed

L15 ANSWER 30 OF 30 GENBANK.RTM. COPYRIGHT 2000

TITLE (TI): Analysis of the Escherichia coli genome VI: DNA sequence of the region from 92.8 through 100 minutes
TITLE (TI): Direct Submission
JOURNAL (SO): Nucleic Acids Res., 23 (12), 2105-2119 (1995)
JOURNAL (SO): Submitted (22-AUG-1994) Guy Plunkett III, Laboratory of Genetics, University of Wisconsin, 445 Henry Mall, Madison, WI 53706, USA. Email: ecoli@genetics.wisc.edu Phone: 608-262-2534 Fax: 608-263-7459
AUTHOR (AU): Burland,V.; Plunkett,G. 3rd; Sofia,H.J.; Daniels,D.L.; Blattner,F.R.
AUTHOR (AU): Plunkett,G. III.

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URRUTIA, Int'l. J. Pancreatology (1997) 22(1):1-14. ISSN:0169-4197.

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URRUTIA, Int'l. J. Pancreatology (1997) 22(1):1-14. ISSN:0169-4197.

WANG et al., Biochim. Biophys. Acta (1994) 1218(3):308-14.

WHELAN et al., J. Steroid Biochem. Mol. Biol. (1996) 58(1):3-12.